REMARKS

Claims 1-5, 7, 9, 11, 15, 16 and 18 are pending in this application. Claims 1-3 and 5 remain pending but are withdrawn from examination as drawn to a non-elected invention.

Applicant has amended claim 4 to promote clarity and to further define the scope of the invention. Amended claim 4 specifies antigenic fragments of SEQ ID NO: 4, wherein said antigenic fragment is not amino acid sequence VLNRLTYNSSSP.

None of the amendments constitutes new matter.

Applicant addresses the Examiner's rejections below:

35 U.S.C. § 112, 2nd paragraph

Claims 4, 7, 9, 11, 15, 16 and 18

Claims 4, 7, 9, 11, 15, 16 and 18 stand rejected under 35 U.S.C. § 112, second paragraph, as being "indefinite". Specifically, the Examiner contends that claim 4 (and therefore, claims dependent therefrom) is indefinite

because: (1) it includes antigenic fragments of an amino acid sequence which is up to 25% different from SEQ ID NO: 4 (i.e., including sequences up to 44 amino acids (25% of the 178 amino acid sequence of SEQ ID NO: 4)) that have no relationship to any sequence disclosed in the present application and (2) it is directed to a protein comprising the antigenic fragments and therefore reads upon any and all proteins.

Claim 4 (and therefore, claims dependent therefrom), as amended, is directed to a protein that comprises the amino acid sequence in SEQ ID NO: 4, an antigenic fragment of that sequence or an amino acid sequence that is at least 75% identical to SEQ ID NO: 4. Accordingly, applicant requests that the Examiner withdraw this rejection.

35 U.S.C. § 112, 1st paragraph

Claims 4, 7, 9, 11, 15, 16 and 18

Claims 4, 7, 9, 11, 15, 16 and 18 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. The Examiner contends that while "the specification fully discloses one species, the protein

consisting of SEQ ID NO: 4...[t]he specification provides no guidance as to what portions of SEQ ID NO: 4 are antigenic, and therefore provides no guidance as to what proteins share antigenic portions with SEQ ID NO: 4." The Examiner contends that those skilled in the art are unable to predict the structure of epitopes or the structure of proteins comprising common epitopes. The Examiner further contends that the specification provides no guidance as to what 25% of SEQ ID NO: 4 may vary without destroying the basic utility of the protein as a virus antigen. The Examiner further states that claim 18 requires a "subunit" of a virus which has in its genome a sequence at least 75% identical to SEQ ID NO: 1 but that the specification does not disclose any physical or chemical characteristics of any subunit of a virus. Applicant traverses on the basis of the foregoing claim amendments and the following remarks.

First, claim 4 (and therefore, claims dependent therefrom), as amended, is directed to a protein that comprises the amino acid sequence in SEQ ID NO: 4, an antigenic fragment of that sequence or an amino acid sequence that is at least 75% identical to SEQ ID NO: 4.

Second, it is submitted that one skilled in the art does not need to know anything about the structure of the epitopes. All that is required is that portions of SEQ ID NO: 4 are tested for antigenic activity. One skilled in the art, faced with determining which portions of SEQ ID NO: 4 are antigenic, would prepare a range of fragments from the sequence and test them for antigenicity. This is a standard procedure performed by those skilled in the art in order to identify antigenic fragments. Accordingly, based on the information disclosed in the specification, one skilled in the art could easily identify antigenic fragments of SEQ ID NO: 4 and therefore the applicant was in possession of the claimed invention.

Third, the Examiner states that the specification provides no guidance as to which 25% of SEQ ID NO: 4 may be varied without destroying its basic utility. It is submitted that such information is not required in order to be in possession of the invention. In order to be in possession of the invention, one skilled in the art must be able to obtain proteins comprising a sequence at least 75% identical to SEQ ID NO: 4. This can be achieved by isolating the

corresponding proteins from other viruses within the same defined group, namely Ljungan viruses. For example, the application discloses three Ljungan viruses, namely 145SL (from which SEQ ID NO: 4 has been obtained), 87-012 and 174F. By comparing the corresponding sequences of 87-012 and 174F to SEQ ID NO: 4 disclosed on page 11 at Table 2 of the specification, it can be determined that the sequences have 82.8% sequence identity. Such comparable sequences indicate that the applicant was in possession of proteins having 75% or more sequence identity to SEQ ID NO: 4 given that the applicant was in possession of Ljungan viruses 87-012 and 174F. Furthermore, by comparing the sequences between the three strains, the versions which can be varied in the sequence will be apparent to those skilled in the art.

Finally, the Examiner has objected to claim 18 due to the use of the term "subunit". The Examiner indicates that the applicant is in possession of three islets but does not consider the applicant to be in possession of a subunit of a virus. Applicant submits that viral subunits are known components of viruses in the same way that a wheel is a known component of a bicycle. Accordingly, the fact that the

applicant is in possession of three viral isolates suggests that the applicant must also be in possession of a viral subunit. The Examiner states that the specification provides no information on the physical or chemical characteristics of the subunits of the viruses. However, such information is not necessary. All that claim 18 requires is that the vaccine comprises a subunit of the virus. Furthermore, on page 6, lines 6-7 of the Office Action, the Examiner states that:

> "Picornaviruses are known to process their polyproteins into a variety of subunits,..."

Accordingly, the Examiner admits that related picornaviruses are known to have subunits. It is submitted that one skilled in the art could easily arrive at a vaccine comprising a subunit of any of the Ljungan viruses disclosed in the present application.

In light of the above comments, applicant submits that the specification provides adequate written description for the claims. Accordingly, applicant requests that the Examiner withdraw this rejection.

35 U.S.C. § 112, 1st paragraph

Claim 4

Claim 4 stands rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that while the specification is enabling for a protein comprising SEQ ID NO: 4 or a polypeptide consisting of an antigenic fragment of SEQ ID NO: 4, it does not reasonably provide enablement for the full scope of proteins comprising antigenic fragments or variant proteins or fragments of the variant proteins. The Examiner contends that the specification provides no guidance regarding what variations may be introduced into the sequence without altering the antigenic nature of the protein, and provides no guidance as to proteins which contain conserved epitopes. Applicant traverses.

Applicant submits that the Examiner stated on page 5, lines 5-7 of the Office Action that:

> "...routine techniques such as oligopeptide mapping would indicate which fragments of SEQ ID NO. 4 have antigenic determinants without undue experimentation...."

Accordingly, the Examiner considers it would be routine for one skilled in the art to identify regions of SEQ ID NO: 4 which comprise antigenic determinants. It is submitted that one skilled in the art having this information would know that sequence variations can be introduced outside the antigenic determining regions of SEQ ID NO: 4 without affecting the antigenic nature of the protein. Furthermore, minor conservative changes to the antigenic determining regions of SEQ ID NO: 4 could be introduced without affecting the antigenic nature of the protein. Although there may be some trial and error in making such modifications, the degree of trial and error is a necessary part of making any change to a protein sequence and would not be considered undue experimentation by those skilled in the art.

Accordingly, one skilled in the art, knowing the antigenic regions of SEQ ID NO: 4, would know where variations of the sequence can be introduced without destroying the antigenic nature of the protein. Accordingly, applicant submits that the specification fully enables the invention of the claims and requests that the Examiner withdraw this rejection.

Claims 7, 9, 11, 15, 16 and 18

Claims 7, 9, 11, 15, 16 and 18 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that in order to use the diagnostic kit recited in claim 7, the specification must enable diagnosis of infection using the components of the kit. The Examiner further contends that in order to enable the pharmaceutical compositions and methods recited in claims 9, 11, 15, 16 and 18, the specification must enable a body-treating method that achieves a beneficial result, using the components of the composition. The Examiner states that while the specification teaches that isolated viruses can be used for serological diagnosis, it provides no evidence that sera of virus-exposed subjects react with SEQ ID NO: 4 to any detectable extent. The Examiner further states that the specification provides no evidence that an immune response directed against SEQ ID NO: 4 has any beneficial effect in preventing or treating diseases. Applicant traverses.

Applicant submits that the Examiner stated on page 5, lines 3-5 of the Office Action that:

> "...[a]ntibodies can be made against SEQ ID NO. 4, and the antibodies would be able to detect one or more polypeptides made during virus infection."

Accordingly, the Examiner believes that antibodies against SEQ ID NO: 4 will be able to detect one or more polypeptides during a viral infection. The one or more polypeptides being detected will comprise SEQ ID NO: 4. Accordingly, it must be the case that one or more polypeptides made during virus infection will be antigenic and cause the production of antibodies, some of which will have an affinity for SEQ ID NO: 4. In particular, the presence of a virus within a body will cause the production of antibodies against a variety of antigenic determinants, including those contained in SEQ ID NO: 4. The sera of the individual will therefore comprise antibodies directed against SEQ ID NO: 4 and the presence of such antibodies can be determined using SEQ ID NO: 4.

The Examiner states that there is no evidence that sera of virus-exposed subjects reacts with SEQ ID NO: 4 to any detectable extent. However, the Examiner states that SEQ ID NO: 4 can be used to raise antibodies. Therefore one

skilled in the art would have no reason to doubt that the diagnostic kit of claim 7 will work.

The Examiner also states that "[p]icornaviruses are known to process their polyprotein into a variety of subunits and only some of the subunits are routinely used for serological purposes" (see page 6, lines 6-7 of the Office Action). The fact that only some subunits are routinely used for serological purposes does not mean that subunits against which an antibody can be raised cannot be used to diagnose viral infection. Instead, it is submitted that the Examiner's statement simply means that some subunits are better than others. There is no evidence to suggest that the subject matter of claim 7 is not enabled.

The Examiner contends that the specification provides no evidence that an immune response directed against SEQ ID NO: 4 has any beneficial effect in preventing or treating a disease. However, an immune response raised against an antigenic component of an infectious agent will, to some extent, have a beneficial effect in preventing or treating a subsequent viral infection. This is the basis of

all traditional vaccines. The possibility that the beneficial effects may be relatively small, and may be complicated by various other factors, does not detract from the basic principle that an immune response to a component of an infectious agent will have a beneficial effect in preventing or treating a subsequent infection. Accordingly, applicant submits that the specification fully enables the invention of claims 7, 9, 11, 15, 16 and 18 and requests that the Examiner withdraw this rejection.

35 U.S.C. § 102(b)

Claims 4, 7, 11 and 15

Claims 4, 7, 11 and 15 stand rejected under 35 U.S.C. § 102(b), as being anticipated by Hyypia *et al.*, "A Distinct Picornavirus Group Identified By Sequence Analysis", *Proc. Natl. Acad. Sci. USA*, 89: 8847-8851 (1992) ("Hyypia"). The Examiner states that Hyypia discloses a picornavirus polypeptide comprising a fragment at about nucleotides 2210-2250 of Figure 2 which is identical to an antigenic fragment of SEQ ID NO: 4 (i.e., a 12-mer sequence (VLNRLTYNSSSP) at positions 141-152 of SEQ ID NO: 4). The Examiner contends

that the polyprotein disclosed in Hyypia meets the limitations of claim 4, as well as the limitations of claims 7, 11 and 15 because they do not require any components other than the protein of claim 4. The Examiner has also cited the following references illustrating the state of the picornavirus art: Rueckert, R.R., "Picornaviridae: the viruses and their replication." Fields Virology, 3rd edition, ed. B.N. Fields et al., Lippincott-Raven Publishers, Philadelphia, pp. 609-654 (1996) and Melnick, J.L., "Enteroviruses: polioviruses, coxsackieviruses, echoviruses, and newer enteroviruses." Fields Virology, 3rd edition, ed. B.N. Fields et al., Lippincott-Raven Publishers, Philadelphia, pp. 655-712 (1996).

Applicant has amended claim 4 (and therefore, claims dependent therefrom) to recite a protein wherein the antigenic fragment is not amino acid sequence VLNRLTYNSSSP. Hyypia discloses the nucleotide sequence of echovirus 22, a distinct member in the family of picornaviruses. Hyypia does not teach a protein that comprises the amino acid sequence in SEQ ID NO: 4, an antigenic fragment of that sequence or an amino acid sequence that is at least 75% identical to SEQ ID

NO: 4, wherein said antigenic fragment is not amino acid sequence VLNRLTYNSSSP. Accordingly, applicant respectfully requests that the Examiner withdraw this novelty rejection.

CONCLUSION

For all the above reasons, applicant requests that the Examiner withdraw all outstanding rejections and grant allowance of the pending claims.

The Examiner is invited to telephone applicant's representatives regarding any matter that may be handled by telephone to expedite allowance of the pending claims.

Respectfully submitted,

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